

AMENDMENTS TO THE CLAIMS

The following listing of claims replaces all prior versions and listings of claims in this application:

1. (Currently Amended) A gel formulation for the transdermal or transmucosal administration of an active agent comprising:

at least one active agent, provided that the active agent is not testosterone alone, and that when the active agent is estrogen, progestin is not present in the formulation in a therapeutically effective amount, and when the active agent is progestin, estrogen is not present in the formulation in a therapeutically effective amount;

a gelling agent; and

a delivery vehicle comprising an alkanol, a polyalcohol and a permeation enhancer in an amount sufficient to provide permeation enhancement of the active agent through mammalian dermal or mucosal surfaces;

wherein the formulation is substantially free of long-chain fatty alcohols, long-chain fatty acids and long-chain fatty esters to avoid undesirable odor and irritation from such compounds during use of the formulation, and wherein the alkanol is present in an amount between about 5 to 80% by weight of the delivery vehicle, the polyalcohol is present in an amount between about 1% to 15% by weight of the delivery vehicle, and the permeation enhancer is present in an amount between about 0.2% to 15% by weight of the delivery vehicle so that the delivery vehicle facilitates absorption of the at least one active agent by the dermal or mucosal surfaces so that transfer or removal of the formulation from such surfaces is minimized.

2. (Canceled)

3. (Currently Amended) The formulation of claim [[2] 1, wherein the active agent is estradiol present in an amount between about 0.01% to 2% of the formulation; the alkanol is present in an amount between about 20 to 65% of the formulation; the polyalcohol is propylene glycol; the permeation enhancer is diethylene glycol monoethyl ether; ~~and further wherein the formulation comprises a gelling agent~~ is present in an amount of between 0.05% to about 4% of the formulation, and the formulation further comprises a neutralizing agent present in an amount

between about 0.05% and 1% of the formulation, and water present in an amount between about 20% to 65% of the formulation.

4. (Original) The formulation of claim 3, further comprising a sequestering agent.
5. (Currently Amended) The formulation of claim [[2] 1, wherein the alkanol is in combination with water to form a hydroalcoholic mixture, the hydroalcoholic mixture is present in an amount of between about 40 to about 98% by weight of the delivery vehicle, and the alkanol is present in an amount of between about 5% to 80% by weight of the mixture, and the water is present in an amount of between about 20% to 95% by weight of the mixture.
6. (Currently Amended) The formulation of claim [[2] 1, wherein the polyalcohol and permeation enhancer are present in a weight ratio of 2:1 to 1:1 and the total amount of polyalcohol and permeation enhancer is not more than 15% of the formulation.
7. (Currently Amended) The formulation of claim 1, wherein the alkanol is a C₂ to C₄ alcohol selected from the group consisting of ethanol, isopropanol, and n-propanol, the polyalcohol is propylene glycol or polypropylene glycol, and the permeation enhancer is a ~~tetraglycol furel~~ or a monoalkyl ether of diethylene ether.
8. (Original) The formulation of claim 1, wherein the active agent is androgen, estrogen, progestin, or a combination thereof.
9. (Original) The formulation of claim 8, wherein the androgen is selected from the group consisting of: testosterone, 17- β -hydroxyandrostenedione, testosterone esters, methyl testosterone, testolactone, oxymetholone, fluoxymesterone, androsterone, androsterone acetate, androsterone propionate, androsterone benzoate, androstenediol, androstenediol-3-acetate, androstenediol-17-acetate, androstenediol-3,17-diacetate, androstenediol-17-benzoate, androstenediol-3-acetate-17-benzoate, androstenedione, sodium dehydroepiandrosterone sulfate, 4-dihydrotestosterone, 5 α -dihydrotestosterone, dromostanolone, dromostanolone propionate, ethylestrenol, nandrolone phenpropionate, nandrolone decanoate, nandrolone furylpropionate,

nandrolone cyclohexanepropionate, nandrolone benzoate, nandrolone cyclohexanecarboxylate, oxandrolone, and stanozolol or any combination thereof.

10. (Original) The formulation of claim 8, wherein the estrogen is selected from the group consisting of: 17 beta-estradiol, estradiol, estradiol benzoate, estradiol 17 beta-cypionate, estriol, estrone, ethynil estradiol, mestranol, moxestrol, mytatrienediol, polyestradiol phosphate, quinestradiol, and quinestrol or any combination thereof.

11. (Previously Presented) The formulation of claim 1, wherein the formulation further comprises at least one of a neutralizing agent; buffering agent, moisturizing agent, humectant, surfactant, antioxidant, emollient, or buffer.

12. (Cancelled)

13. (Previously Presented) A method for treating hormonal disorders in a subject, the method comprising administering to a subject in need of such treatment the gel formulation of claim 1 wherein the active agent is a hormone which is effective for treating at least one symptom of the hormonal disorder selected from the group consisting of hypogonadism, female menopausal symptoms, female sexual dysfunction, hypoactive sexual desire disorder, and adrenal insufficiency, and wherein the administration of the formulation decreases the frequency of at least one clinical symptom of the hormonal disorder.

14. (Cancelled)

15. (Original) The method of claim 13, wherein the active agent is an androgen, estrogen, progestin, or a combination thereof.

16. (Original) The method of claim 13, wherein the androgen is selected from the group consisting of: testosterone, 17- β -hydroxyandrostenedione, testosterone esters, methyl testosterone, testolactone, oxymetholone, fluoxymesterone, androsterone, androsterone acetate, androsterone propionate, androsterone benzoate, androstenediol, androstenediol-3-acetate, androstenediol-17-acetate, androstenediol-3,17-diacetate, androstenediol-17-benzoate,

androstenediol-3-acetate-17-benzoate, androstenedione, sodium dehydroepiandrosterone sulfate, 4-dihydrotestosterone, 5 adihydrotestosterone, dromostanolone, dromostanolone propionate, ethylestrenol, nandrolone phenpropionate, nandrolone decanoate, nandrolone furylpropionate, nandrolone cyclohexanepropionate, nandrolone benzoate, nandrolone cyclohexanecarboxylate, oxandrolone, and stanozolol or any combination thereof.

17. (Original) The method of claim 16, wherein the subject is a female subject, the active agent is testosterone and the therapeutically effective dosage of testosterone is from about 2.2 milligrams to about 0.88 grams each 24 hours.

18. (Original) The method of claim 16, wherein the subject is a female subject, the active agent is testosterone, and further wherein the method increases serum levels of the testosterone to about 142 nanograms per deciliter.

19. (Original) The method of claim 16, wherein the subject is a female subject, the active agent is testosterone, and further wherein the method increases serum levels of the testosterone to about 17 picograms per milliliter.

20. (Original) The method of claim 15, wherein the estrogen is selected from the group consisting of: 17 beta-estradiol, estradiol, estradiol benzoate, estradiol 17 beta-cypionate, estriol, estrone, ethynil estradiol, mestranol, moxestrol, mytatrienediol, polyestradiol phosphate, quinestradiol, and quineestrol or any combination thereof.

21. (Original) The method of claim 15, wherein the progestin is selected from the group consisting of: allylestrenol, anagestone, chlormadinone acetate, delmadinone acetate, demegestone, desogestrel, dimethisterone, dydrogesterone, ethynilestrenol, ethisterone, ethynodiol, ethynodiol diacetate, flurogesterone acetate, gestodene, gestonorone caproate, haloprogestosterone, 17-hydroxy-16-methylene-progesterone, 17 alpha -hydroxyprogesterone, 17 alpha-hydroxygesterone caproate, lynestrenol, medrogestone, medroxyprogesterone, megestrol acetate, melengestrol, norethindrone, norethindrone acetate, norethynodrel, norgesterone, norgestimate, norgestrel, norgestrienone, 19-norprogesterone, norvinisterone, pentagestrone,

progesterone, natural progesterone, promegestone, quingestrone, and trengestone or any combination thereof.

22. (Original) The method of claim 20, wherein the subject is a female subject, the active agent is estradiol and the therapeutically effective dosage of estradiol is from about 0.375 to about 1.5 milligrams each 24 hours.

23. (Original) The method of claim 20, wherein the subject is a female subject, the active agent is estradiol and the free serum concentration of estradiol is increased to about 8.8 nanograms per deciliter.

24. (Original) The method of claim 20, wherein the subject is a female subject, the active agent is estradiol, and further wherein the method increases serum levels of estrone to about 10.4 nanograms per deciliter.

25. (Original) The method of claim 20, wherein the subject is a female subject, the active agent is estradiol, and further wherein the method increases serum levels of estrone to about 193 nanograms per deciliter.

26. (Original) The method of claim 13, wherein the active agent is a combination of two different active agents administered concurrently.

27. (Original) The method of claim 13, wherein a female subject is treated for hypogonadism, female menopausal symptoms, or female sexual disorder, and the formulation comprises testosterone in combination with a further active agent selected from the group consisting of estrone, estradiol, 17 β estradiol, ethynil estradiol, estriol, succinate, estriol dihexanate and estriol sulfamate.

28. (Original) The method of claim 13, wherein a female subject is treated for hypogonadism or female menopausal symptoms, and the active agent includes estradiol in combination with a progestin.

29. (Original) The method of claim 13, wherein a male subject is treated for hypogonadism, and the active agent includes at least one androgen.

30. (Original) The method of claim 13, wherein the at least one androgen includes methyltestosterone in combination with methandrostenolate.

31. (Original) The method of claim 13, wherein the method includes treating a subject for adrenal insufficiency, and the active agent includes dehydroepiandrosterone (DHEA).

Claims 32. to 36. (Cancelled)

37. (Original) A formulation for the transdermal or transmucosal administration of an active agent comprising:

at least one active agent; and

a delivery vehicle comprising an alkanol, a polyalcohol and a permeation enhancer of a tetraglycol furol in an amount sufficient to provide permeation enhancement of the active agent through mammalian dermal or mucosal surfaces.

38. (Original) The formulation of claim 37, wherein the formulation is substantially free of long-chain fatty alcohols, long-chain fatty acids, and long-chain fatty esters to avoid undesirable odor and irritation from such compounds during use of the formulation.

39. (Canceled)

40. (Currently Amended) The formulation of claim ~~[[39]]~~ 37, wherein the alkanol is in combination with water to form a hydroalcoholic mixture, the hydroalcoholic mixture is present in an amount of between about 40 to about 98% by weight of the delivery vehicle, and the alkanol is present in an amount of between about 5% to 80% by weight of the mixture, and the water is present in an amount of between about 20% to 95% by weight of the mixture.

41. (Currently Amended) The formulation of claim [[39]] 37, wherein the polyalcohol and permeation enhancer are present in a weight ratio of 2:1 to 1:1 and the total amount of polyalcohol and permeation enhancer is not more than 15% of the formulation.

42. (Currently Amended) The formulation of claim [[39]] 37, wherein the alkanol is a C₂ to C₄ alcohol selected from the group consisting of ethanol, isopropanol, and n-propanol, and the polyalcohol is propylene glycol or polypropylene glycol.

43. (Original) The formulation of claim 37, wherein the active agent is androgen, estrogen, progestin, or a combination thereof.

44. (Original) The formulation of claim 43, wherein the androgen is selected from the group consisting of: testosterone, 17-β-hydroxyandrostenedione, testosterone esters, methyl testosterone, testolactone, oxymetholone, fluoxymesterone, androsterone, androsterone acetate, androsterone propionate, androsterone benzoate, androstenediol, androstenediol-3-acetate, androstenediol-17-acetate, androstenediol-3,17-diacetate, androstenediol-17-benzoate, androstenediol-3-acetate-17-benzoate, androstenedione, sodium dehydroepiandrosterone sulfate, 4-dihydrotestosterone, 5 α-dihydrotestosterone, dromostanolone, dromostanolone propionate, ethylestrenol, nandrolone phenpropionate, nandrolone decanoate, nandrolone furylpropionate, nandrolone cyclohexanepropionate, nandrolone benzoate, nandrolone cyclohexanecarboxylate, oxandrolone, and stanozolol or any combination thereof.

45. (Original) The formulation of claim 43, wherein the estrogen is selected from the group consisting of: 17 beta-estradiol, estradiol, estradiol benzoate, estradiol 17 beta-cypionate, estriol, estrone, ethynil estradiol, mestranol, moxestrol, mytatrienediol, polyestradiol phosphate, quinestradiol, and quinestrol or any combination thereof.

46. (Currently Amended) The formulation of claim 37, wherein the formulation further comprises at least one of a ~~gelling agent~~, neutralizing agent; buffering agent, moisturizing agent, humectant, surfactant, antioxidant, emollient, or buffer.

47. (Original) The formulation of claim 37, wherein the formulation is in the form of a gel, lotion, cream, spray, aerosol, ointment, emulsion, suspension, liposomal system, lacquer, patch, bandage, or occlusive dressing.

Claims 48. to 55. (Cancelled)

56. (Previously Presented) A kit for treating a subject for increasing serum levels of an active agent in a subject comprising: a gel formulation according to claim 1; and
a container that retains the formulation and includes a dispenser for releasing or applying a predetermined dosage or volume of the formulation upon demand.

57. (Original) The kit of claim 56, wherein the dispenser automatically releases the predetermined dosage or volume upon activation by a user.

58. (Original) The kit of claim 56, wherein the dispenser is a pump.

59. (Previously Presented) A gel formulation for the transdermal or transmucosal administration of an active agent comprising:
at least one active agent comprising dehydroepiandrosterone (DHEA);
a gelling agent; and
a delivery vehicle comprising an alkanol, a polyalcohol and a permeation enhancer in an amount sufficient to provide permeation enhancement of the active agent through mammalian dermal or mucosal surfaces.

60. (Currently Amended) A gel formulation for the transdermal or transmucosal administration of an active agent for treating a hormonal disorder in a subject comprising:
at least one active agent which is effective for treating at least one symptom of the hormonal disorder and in an amount effective for that purpose, provided that the active agent is not testosterone alone, and that when the active agent is estrogen, progestin is not present in the formulation in a therapeutically effective amount, and when the active agent is progestin, estrogen is not present in the formulation in a therapeutically effective amount;
a gelling agent; and

a delivery vehicle comprising an alkanol, polypropylene glycol, and a permeation enhancer of a ~~tetraglycol furol or a monoalkyl ether of diethylene ether~~ in an amount sufficient to provide permeation enhancement of the active agent through mammalian dermal or mucosal surfaces, wherein the alkanol is present in an amount between about ~~5 to 80~~ 20 to 65% by weight of the delivery vehicle, the polypropylene glycol is present in an amount between about 1% to 15% by weight of the delivery vehicle, and the permeation enhancer is present in an amount between about 0.2% to 15% by weight of the delivery vehicle, with the polyalcohol and permeation enhancer being present in a weight ratio of 2:1 to 1:1, and with the alkanol being ethanol, isopropanol, or n-propanol, so that the delivery vehicle facilitates absorption of the at least one active agent by the dermal or mucosal surfaces; and

wherein the formulation is substantially free of long-chain fatty alcohols, long-chain fatty acids and long-chain fatty esters to avoid undesirable odor and irritation from such compounds during use of the formulation and the delivery vehicle facilitates absorption of the at least one active agent by the dermal or mucosal surfaces so that transfer or removal of the formulation from such surfaces is minimized.

61. (New) A kit for treating a subject for increasing serum levels of an active agent in a subject comprising: a gel formulation according to claim 37; and

a container that retains the formulation and includes a dispenser for releasing or applying a predetermined dosage or volume of the formulation upon demand.

62. (New) The kit of claim 61, wherein the dispenser automatically releases the predetermined dosage or volume upon activation by a user.

63. (New) The kit of claim 61, wherein the dispenser is a pump.